UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,025	10/04/2005	Vishwanath R. Lingappa	UCSF.004.01US	6909

22798 7590 11/30/2007

QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.
P O BOX 458
ALAMEDA, CA 94501

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/512,025	LINGAPPA, VISHWANATH R.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I, claim 1, in the response of 09/24/07 is acknowledged.

The traverse is on the ground that it would not be a serious burden to search the different inventions. The response also asserts that the antibody taught by Lee et al does not anticipate the claimed antibody.

The response has been considered but is not found to be persuasive for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions listed as groups 1-10 do not relate to a single general inventive concept because the shared technical feature of the claimed invention, an antibody substantially specific for a conformer of prostatic acid phosphastase lacks novelty and does not make a contribution over the prior art. An antibody substantially specific for a conformer of prostatic acid phosphastase is the same as the antibody taught by Lee et al, of record, for reasons already of record, or by Janckila et al, 1997, Hybridoma, 16 (2): 175-182, or Miyazaki et al, 2002, Hybridoma and hybridomics, 21(2): 191-195, which teach monoclonal antibodies specific for a conformational determinant of native, tartrate-resistant acid phosphatase (see 103 below).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 1 is indefinite, for the use of the language "conformer". Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "conformer" in claim1 is used by the claim to mean "a conformation determinant", while the accepted meaning is "a mold, usually of plastic material, used in plastic surgical repair" (Stedman's Medical Dictionary, 25th Ed, 1990, p.342). The term is indefinite because the specification does not clearly redefine the term.

2. Claim 1 is indefinite for the use of the language "disease-related". It is not clear what type of relationship is referred to.

3. Claim 1 is indefinite for the use of the language "substantially", which is a relative term.

Claim Rejections - 35 USC § 112, First Paragraph, Scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting a conformation determinant of a prostatic acid phosphatase in prostate cancer, does not reasonably provide enablement for a method for identifying a one or more **prostate disease**-related conformer of prostatic acid phosphatase, said method comprising contacting a biological fluid sample from a patient with a disease of the prostate with a plurality of conformer-specific antibodies to prostatic acid phosphatase, using any **control sample**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

To comply with the enablement requirement of 35 U.S.C. § 112, first paragraph, the specification must enable one skilled in the art to make and use the claimed invention without undue experimentation. The claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows: (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The specification discloses that the secreted form of prostatic acid phosphatase, as found in blood is specific for prostate cancer, in particular metastatic prostate cancer (p.1, paragraph before last).

A prostate disease encompasses any diseases from the prostate, which is not necessary prostate cancer.

One cannot predict that any disease of the prostate would produce prostatic acid phosphatase having specific conformation related to prostate cancer, in view that different diseases have different etiology and characteristics, and would not predictably produce the secreted form of prostatic acid phosphatase, as found in blood of patients having prostate cancer.

Further, one cannot predict that any control sample could used in the claimed method, because the antibody binding in such control sample would not necessarily be different from that of the tested biological fluid of prostate cancer patient. Such control sample could encompass, for example, seminal fluid, or spleen from hairy cell leukemia, which also express bands 2, and 5 isozymes of prostatic acid phosphatase, found in serum of prostate carcinoma patients, having bone metastasis (Sun et al, 1981, Clin Chem, 27: 1742-1744, especially figure 1 on page 1743, and p.1742, second column, last 9 lines of first paragraph).

MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is

unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, there would be an undue quantity of experimentation required for one of skill in the art to practice the claimed invention, that is commensurate in scope of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bull et al, 2000, Immunol Letters, 70(3): 143-149, in view of Lee et al, 1984, Biochem J, 223: 871-877, of record, and Janckila et al, 1997, Hybridoma, 16 (2): 175-182.

Claim 1 is drawn to: A method for identifying a one or more prostate disease-related conformer of prostatic acid phosphatase, said method comprising:

contacting a biological fluid sample from a patient with a disease of the prostate with a plurality of conformer-specific antibodies to prostatic acid phosphatase;

detecting substantially specific binding of said antibodies to prostatic acid phosphaiase conformers in said sample as compared to a control sample as indicative of the presence of one or more disease-related conformer of prostatic acid phosphatase in said sample.

Bull et al teach an antibody (5C1) that binds human prostatic acid phosphatase (P-AP), and tartrate-resistant acid phosphatase (abstract, table 1 on page 5). Bull et al teach that 5C1 is positive in ELISA, but negative in immunocytochemistry, and that ELISA does not perturb the **conformation of the target epitope**, whereas immunocytochemistry can modify or mask antigenic determinant (p.7, third paragraph). Bull et al teach that although 5C1 does not react with bovine acid phosphatase, it cross-reacts with potato acid phosphatase in ELISA, indicating reactivity to conformationnally similar epitopes (abstract, p.7, fourth paragraph).

Bull et al do not teach a method for identifying a conformer of prostatic acid phosphatase related to prostate cancer, using a biological fluid sample of a patient having prostate cancer.

Lee et al teach that **activity** of **prostatic acid phosphatase (PAP)** in **serum** is elevated patients with metastatic prostate cancer, and that there are known immunoassay for the detection of serum PAP for diagnosis of prostate cancer (p.223, first column). Lee et al teach polyclonal antibodies specific for the **native** prostatic acid phosphatase (figure 2 and table 2 on page 875). Lee et al teach making fragments of prostatic acid phosphatase, that retain intact disulphide bonds, which prevent unfolding of the polypeptide (p.876, first column, last paragraph). Lee et al teach that thus the fragments contain the entire antigenic active sites of the native, non-denatured prostatic acid phosphatase (p.876, first column, last paragraph, bridging second column, second column, second paragraph). Lee et al teach that in a competitive binding assay, a large excess of these fragments are required to inhibit the binding of these antibodies to the native prostatic acid phosphatase, and that such requirement of an increase in concentration of the fragments is necessary to achieve the characteristic folding of the antigenic sites of the native prostatic acid phosphatase (p.876, second column, third paragraph, figure 2 and table 2 on page 875). From the teaching of Lee et al, it is clear that the antibodies to native prostatic acid phosphatase are to the conformation or shape of the native prostatic acid phosphatase, because an increase in concentration of the fragments is necessary to achieve the characteristic **folding** of the antigenic sites **of the native** prostatic acid phosphatase to displace the binding of the antibodies to the native prostatic acid phosphatase.

Janckila et al teach monoclonal antibody 14G6 that reacts specifically with **native**, active tartrate-resistant acid phosphatase (TRAP), and not with denatured TRAP (abstract, p.175, figure

2 on page 177). Janckila et al teach that the antibody reacts **with conformational determinant** on the tartrate resistant acid phosphatase (TRAP) (abstract, p.175, figure 2 on page 177), as shown by immunoprecipitation of only native, active TRAP, and abolishment of the antibody reactivity to heat-denatured TRAP in a variety of immunoassays (p.179, third paragraph). Janckila et al teach that the antibody reacts with the antigen in enzyme immunoassay, and immunoprecipitation, but not in denaturing Western blot or immunohistochemistry (p.177-179). Janckila et al teach that the antibody to a denatured epitope of TRAP is well suited for **denaturing** Western blot and immunohistochemistry, but is ill-suited for immunoassay of active TRAP (abstract, p.175, second column).

The 5C1 antibody taught by Bull et al clearly is specific for the conformation determinant of prostatic acid phosphatase (PAP), and does not bind to the denatured epitope of PAP, in view that it is ELISA restricted, which immunoassay does not perturb the conformation of the target epitope, as taught by Bull et al, as compared to denaturing immunohistochemistry, as taught by Bull et al, and Janckila et al.

It would have been prima facia obvious to one of ordinary skill in the art at the time the invention was made to use the antibody to native, active prostatic acid phosphatase (PAP) taught by Bull et al or Lee et al, which bind to the conformation determinant on native PAP, to detect PAP in serum of prostate cancer patients, because: 1) the activity of PAP in serum is increased in metatastic prostate cancer, as taught by Lee et al, 2) antibody to the conformation determinant of native, active PAP is more suitable for immunoassay of the serum, as compared to antibody to a denatured epitope of PAP, in view of the teaching of Bull et al, and Janckila et al, and 3)

antibody to native, active PAP would detect PAP that retains its activity, which activity is shown to be increased in metastatic prostate cancer, as taught by Lee et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, LARRY HELMS can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
November 15, 2007

/Larry R. Helms/

Supervisory Patent Examiner